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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/648,813	08/25/2003	Erkki Ruoslahti	066821-0233	5267

41552 7590 11/16/2007

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EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
11/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/648,813	RUOSLAHTI ET AL.	
	Examiner	Art Unit	
	Lei Yao, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *200-298* is/are pending in the application.

4a) Of the above claim(s) *248-251,258,259,283-286,293-298* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *200-212,214-226,228-241,243-247,252-257,260-276,278-282,287-292* is/are rejected.

7)☒ Claim(s) *213,227,242, 277* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *6/26/2007*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Arguments and Amendments

The Amendment filed on 9/14/2007in response to the previous Non-Final Office Action 2/20/2007) is acknowledged and has been entered.

Claims 200-298 are added and pending. Claims 248-251, 258-259, 283-286, 293-294 are corresponding to originally presented claims 114-117, 124-125 and 139-140 and 143-144 drawn to a conjugate comprising SEQ ID NO: 1 linked to nucleic acid, a small molecule, a virus, or a phage, have been withdrawn as non-elected species from consideration. It is also noted that newly submitted claims 295-298 directed to an invention that is independent or distinct from the invention originally claimed because the claims are drawn to a fusion protein or bifunctional peptide comprising CREAK fused to heterologous peptide that are not originally elected species or invention. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 295-298 are also withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Thus, claims 200-247, 252-257, 260-282, and 287-292 are under consideration.

Rejections/Requirement Withdrawn

1. Sequence Requirements is withdrawn in view of applicant's argument.

2. The rejection of claim 102-113, 118-123, and 188-199 recites the limitation "said peptide " in claim 102 because of no insufficient antecedent basis for this limitation in the claim is withdrawn in view of the cancellation of the claims.

3. The rejection of claims 99-107, 110-113, 118-123 and claims 178-186, 188-198 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of cancellation of the claims. Newly added claims are subjected to the same rejection (see below).

4, The rejection of claims 99-107, 110-113, 118-123, 178-186, 188-198 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the peptide, CREKA of SEQ ID NO:1, does not reasonably provide enablement for the other peptides having 7-100 amino acid

residues comprising CREKA of SEQ ID NO:1 and a conjugate comprising the peptides above is withdrawn in view of cancellation of the claims. Newly added claims are subjected to the same rejection (see below).

The following is a New Ground of rejection-based on the newly added claims

The following is a quotation of the **first paragraph** of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description:

Claims 200-212, 214-226, 228-241, 243-247, 252-257, 260-276, 278-282, and 287-292 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a peptide comprising CREKA (SEQ ID NO: 1), having less than 7, 8, 9, 10, 12, 15, 20, 25, 30, 35, 40, 50, or 100 amino acid residues, wherein peptides selectively homes to tumor vasculature or selectively binds collagen, or a conjugate comprising a therapeutic agent linked to the peptide above. Thus, the claims are inclusive of a genus of peptides having amino acid residues between 6-100 at length comprising five amino acids, CREKA (SEQ ID NO: 1) and a genus of conjugates linked to the peptides above. However, the specification (page 73-75) only reasonably conveys one species of homing molecule, a peptide, CREKA (SEQ ID NO:1) associated with collagen binding in the tumor vasculature. The term "comprising" in the claims are open-ended. It expands the sequence of SEQ ID NO: 1 to include additional non-disclosed amino acid residues (from 1-95) outside of the sequence shown in SEQ ID NO: 1. Therefore, the instant claims encompass in their breadth any peptide comprising amino acid sequence disclosed in SEQ ID NO: 1 and additional unknown amino acid residues. The specification neither provides any peptide above towards a genus of the peptides having amino acid residues 6-100 comprising CREKA, SEQ ID NO: 1, nor sufficient enabling description of those

peptides associated with collagen binding and homing activities. Description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features and representative number of the species that are common to the genus of homing peptides (less than 6-100 residues) comprising sequence CREKA (SEQ ID NO: 1), which homes to tumor vasculature and selectively binds to collagen. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus associated with claimed activities, and because the genus is highly variant, the disclosure of peptide CREKA (SEQ ID NO: 1) is insufficient to describe the genus having more amino acids attached to either or both sides of the peptide maintaining such claimed function. Thus, one of skill in the art would reasonably conclude that the inventor(s), at the time the application was filed, **did not have** possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan could not envision the detailed chemical structure(s) of the encompassed genus of *a* homing peptides or conjugates having less than 7, 8, 9, 10, 12, 15, 20, 25, 30, 35, 40, 50, or 100 amino acid residues comprising CREKA peptide (SEQ ID NO: 1), which could maintain the same functiona as

CREKA. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only the peptide, CREKA (SEQ ID NO: 1) and conjugate comprising therapeutic agent linked to the peptide of SEQ ID NO: 1, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112 paragraph 1" Written Description" Requirement.

Previous response to applicant's argument dated 12/19/2006 is also maintained for the reason of record as set forth below and in the Office action dated 2/20/2007.

Scope of Enablement

Claims 200-212, 214-226, 228-241, 243-247, 252-257, 260-276, 278-282, and 287-292 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the peptide, CREKA of SEQ ID NO: 1, homing to tumor vasculature or selectively binding collagen and a conjugate comprising the peptide, CREKA (SEQ ID NO: 1), linked to a cytotoxic agent or anti-angiogenic agent, does not reasonably provide enablement for the other peptides having less than 7, 8, 9, 10, 12, 15, 20, 25, 30, 35, 40, 50, or 100 amino acid residues comprising CREKA of SEQ ID NO:1 and a conjugate comprising the peptides above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factor considered when determining if the disclosure satisfies the enablement requirement and whether any is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of necessary experimentation claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re wands,* 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir.1988).

The claims are broadly drawn to a homing peptide having less than 7, 8, 9, 10, 12, 15, 20, 25, 30, 35, 40, 50, or 100 amino acid residues comprising five amino acids CREKA (SEQ ID NO:1) or a conjugate comprising the peptide having the amino acid sequence less than 7, 8, 9, 10, 12, 15, 20, 25, 30, 35, 40, 50 residues comprising linked to a therapeutic agent comprising a cytotoxic agent or anti-angiogenic molecule. To satisfy the requirement of 112, 1st paragraph, it is necessary that the specification provides an enabling disclosure of how to make and use a claimed invention. The specification teaches only one species of homing molecule, a peptide, CREKA (SEQ ID NO:1) associated with collagen binding in the tumor. The specification does not teach any peptide at any length (7-100 amino acids) comprising CREKA would retain the activity of binding to collagen and homing to tumor vasculature. The specification does not provide any working example or guideline, which enable any conjugate of therapeutic agent linked to the peptide above comprising CREKA (SEQ ID NO: 1) in the claims, which could binds to collagen, or homes to tumor vasculature and maintain the therapeutic function. Thus, one skilled in the art would not know how to use or even make a peptide based on the claims for tumor vasculature homing and binding to collagen without undue experimentation.

It is well known in the art that proteins are folded 3-dimensional structures, the function and stability of which are directly related to a specific conformation (Mathews and Van Holde, Biochemistry, 1996, pp. 165-171). In any given protein, amino acids distant from one another in the primary sequence may be closely located in the folded, 3-dimensional structure (Mathews and Van Holde, Biochemistry, 1996, pp. 166, figure 6.1). It is also know in the art that even a single modification or substitution in a protein sequence can alter the protein function. Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of

the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (Burgess et al, Journal of Cell biology, Vol 111, p2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagines, does not affect biological activity while the replacement with serine or glutamic acid sharply reduce the biological activity of the mitogen (Lazar et al., Molecular and Cellular Biology, vol 8, p1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of the protein.

Furthermore, Shimkets et al., (WO200192523, Publication date, 12/6/2001, see search result provided before) teach a peptide having 52 amino acid residues comprising CREKA of SEQ ID NO: 1, which is involved in diagnosing preventing or treating cardiovascular, neurodegenerative, or proliferative diseases. Shimkets et al., do not record the peptide having function of homing to tumor vasculature and binding to collagen. Thus, one skilled in the art has not recognized a peptide having less than 100 amino acids at length comprising amino acids CREKA would bind to a collagen and homing to tumor because treating disease like neurodenerative disease do not require binding or homing to tumor vascular.

No direction, guidance, or working example is provided in current specification to assist one skilled in the art using the claimed peptides having less than 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, 50, or 100 or a conjugate having less than 7, 8, 9, 10, 15, 20, 25, 30, 35, 40, and 50 amino acid residues comprising 5 basic amino acids CREKA (SEQ ID NO: 1 for binding to a collagen and homing to tumor vasculature. In view of the lack of the predictability of the art to which the invention pertains as evidenced by the arts taught above, one skilled in the art would be forced into under experimentation in order to practice the claimed invention.

Previous response to applicant's argument that applies to the new claims is also maintained for the reason of record as set forth in the Office action dated 2/20/2007.

Response to applicant's argument filed on August 20, 2007, that applies to the new claims:

The response filed 8/20/2007 and 9/14/2007 has been carefully considered but is deemed not to be persuasive. Regarding to the written description rejection, applicant states (middle of page 8) that

> Applicants respectfully maintain that the specification teaches a peptide "comprising" CREKA (SEQ ID NO: 1). In particular, the CREKA (SEQ ID NO: 1) peptide was identified using a phage display library that was injected into mice and recovered from breast tumor tissue (Example 1, pages 67-70). A peptide library was used, with the peptide expressed on the surface of the phage as a fusion with a phage protein, in particular the product of gene III. Such a peptide-gene III fusion protein is exemplary of a peptide "comprising" CREKA (SEQ ID NO: 1).

In response, application is claiming an entirety genus of the peptides having 5-100 amino acids comprising amino acid sequence of SEQ ID NO: 1 (CREKA) and the conjugates comprising the peptides having the homing or collagen binding ability. However, the specification only provides one species that is CREKA peptide gene-III fusion protein, which exhibits homing or binding ability in phage display. No any other peptide having less 100 amino acids comprising CREKA as claimed has been disclosed or suggested in the application. Because the genus is highly variant, the disclosure of peptide CREKA (SEQ ID NO: 1) linked to a gene III protein is insufficient to describe the genus having more amino acids attached to either or both sides of the peptide maintaining such claimed function. Thus, one of skill in the art would reasonably conclude that the inventor(s), at the time the application was filed, did not have possession of the broadly claimed invention.

Applicant further argues the phage display technique and emphasizes that fusion peptide fused to a region of pIII or pVIII would display more than 8 amino acid peptides (page 90

> Smith et al. describes that for gene VIII (not gene III), displaying a peptide of more than about eight amino acids will not support phage production unless it is supplemented by wild type pVIII molecules. The supplementation with wild type pVIII results in mosaics displaying both wild type pVIII and pVIII fusions with displayed peptides. Similarly, certain forms of gene III fusions, in which the foreign peptide replaces the N-terminal domain of pIII, also requires coexpression with complete pIII molecules, resulting in mosaic virions. In both cases, the mosaics support phage production.

In response, first, using phase display for screening a homing molecule or binding partner is already known in the art, many molecules are screened using the technique by fusing a homing peptide with a region of such molecule (pIII or pVIII), which does not support applicant having a possession of a genus of peptides with any sequence fused to the 5 amino acids CREKA (SEQ ID NO: 1) with any length between 7-100 amino acids at any location because applicant provides neither the peptide (except pIII for screen) linked to CREKA, nor objective evidence showing any peptide (except pIII) fused to the CREKA

that could maintain or alter the function of CREKA. Second, regarding with the teaching of Smith et al on phage display more than 8 amino acids supplemented by wild type pVIII molecules, instant specification does not provide clear information that in the process of screening the tumor homing molecule or collagen binding molecule wild type pVIII molecule was supplemented, and no more than 8 amino acids of the homing molecules were identified in this application. Thus, application was filed, did not have possession of the claimed invention. In addition, again, disclosing the CREKA fused to part of pIII would not be enough for representing a genus of the claimed invention that includes any peptide having 7-100 amino acids comprising CREKA sequence.

Applicant on page 10 further argue that

> Regarding the recited size limitations and functional activity, Applicants respectfully maintain that the claims do not include non-functional variants but only those peptides or conjugates comprising CREKA (SEQ ID NO: 1), having a length of less than 100 residues, and that selectively home to tumor vasculature and selectively bind collagen. Thus, the claims are directed to peptides and conjugates and specifically recite size limitations, having a length of less than 100 residues or shorter recited sizes, and functional activity, selectively homing to tumor vasculature and selectively binding collagen, of the peptides comprising CREKA (SEQ ID NO: 1).

In response, again, this written description rejection is based on applicant having no possession of the claimed invention. Although functional language is limited claimed peptide bound to collagen or homing to the tumor vasculature, the peptide could extend about 20 times of functional peptide CREKA in its length, which could include an known or unknown collagen binding or tumor homing motif which is not invented by applicant. In another word, the collagen binding or homing of claimed peptides may not be contributed by CREKA sequence in thhis case. Because broadly claimed peptides have not been supported in this application, one skilled in the art would not be convinced that inventor(s), at the time the application was filed, had possession of the claimed invention.

Thus, applicant's argument has not been found persuasive, and the rejection is maintained for the reasons of record and is made again as set forth above.

Regarding to the enablement rejection, applicant argues (page 10-11) that

> claimed peptides and conjugates recite the CREKA sequence and require the functional activity of the CREKA peptide of selective homing to tumor vasculature and selective binding to collagen and the description in Burgess et al. and Lazar et al. of amino acid substitutions in the binding site

> of acidic FGF and TGF that alter activity are not relevant to the claimed peptides and conjugates, which recite the CREKA peptide that has the functional activity of selectively homing to tumor vasculature and selectively binding collagen.

In response, claimed invention does not intend to change the amino acid sequence of CREKA, instead of including additional up to 95 additional amino acids to either side of CREKA. Applicant does not provide any objective evidence, direction, or predictability showing such proteins or peptides with variant structures would perform the same function as CREKA attached to pIII in the phage display because applicant does not seem concern the secondary structure of the fusion protein.

Applicant also argues (page 11) that

> Shimkets et al. reference describes a peptide comprising CREKA but does not record the peptide as having the function of homing to tumor vasculature and binding to collagen. Shimkets et al. that the 11,491 open reading frames identified can be used in the treatment of a laundry list of diseases and conditions is not relevant to the claimed peptides, which recite the specific structure of the CREKA peptide and the functional activity of selectively homing to tumor vasculature and selectively binding collagen.

In response, Shimkets is relevant with the current invention because neither applicants or skilled artisan have proved that any peptides having 7-100 amino acids comprising only 5 amino acids of CREKA would have the same homing or collagen binding activity as CREKA. One skilled in the art including inventor have studies and published homing molecules for years and most of the molecules are small peptides with less about 10 amino acids for maintaining the specificity of the tumor vascular homing ability. If applicant has the objective evidence that show any large peptide comprising CREKA having the ability to collagen binding or homing to vasculature the Office would like to give a reconsideration for the current rejection.

Applicant also argues (page 12) that

> one skilled in the art would readily know how to add amino acids to the amino or carboxyl terminus of a CREKA peptide and test the ability of the peptide to selectively home to tumor vasculature and selectively bind collagen using, for example, the methods taught in the specification (see Examples 1-3, pages 67-78). The claims are thus directed to peptides and conjugates and specifically recite size limitations, having a length of less than 100 residues or shorter recited sizes, and functional activity, selectively homing to tumor vasculature and selectively binding collagen, of the peptides comprising CREKA (SEQ ID NO: 1).

In response, although the specification teaches a screening method that has identified peptide CREKA having homing and collagen binding activities, the specification does not give enough direction or guideline to one skilled in the art that any peptide extending 6-95 amino acids from CREKA peptide could perform the same function as the CREKA because again, the activity in the peptides having a structure with up to 95% amino acid difference from the base sequence CREKA is unpredictable and would require undue experimentation and instant specification does not provide any example or objective evidence indicating that such claimed peptide would maintain the activity for tumor homing or collagen binding.

Thus, applicant's argument has not been found persuasive, and the rejection is maintained for the reasons of record and is made again as set forth above.

Claim Objections

Claims 213, 227, 242, 277 are objected to as being dependent from rejected base claims. These claims appear to be allowable if the claims are rewritten in closed language as base claims, i.e. An isolated peptide consisting of the amino acid sequence of SEQ ID NO: 1 and a conjugate comprising a cytotoxic or anti-angiogenic agent linked to the homing molecule consisting of the amino acid sequence of SEQ ID NO: 1.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lei Yao,
Examiner
Art Unit 1642

LY

SHANON FOLEY
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